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KING & SPALDING LLP
1180 PEACHTREE STREET
ATLANTA, GA 30309-3521

EXAMINER	
SAUNDERS, DAVID A	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/754,456	MULLIS, KARY B.	
	Examiner	Art Unit	
	David A. Saunders, PhD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7,13-18,20 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *20* is/are allowed.

6)☒ Claim(s) *1-4,7,13-18 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

AMENDMENT ENTRY

Amendment of 3/8/07 has been entered. Claims 1-4,7,13-18 and 20-21 are pending. Claims 1-4,7,13-18 and 20-21 are under examination.

The amendment has entered no new matter.

OBJECTION(S)/REJECTION(S) OF RECORD WITHDRAWN

The rejection of claim(s) 1 and 20 under 35 USC 112, 2nd paragraph.

The rejection of claim(s) 20 under 35 USC 112, 1st paragraph.

The prior art rejection under 102 based upon Sallberg, due to applicant's amendment of claim 1. The Office will not presently employ Sallberg (5,869,232) in an obviousness rejection (as in the case further infra with the Krsmanovic et al and Marinkovich references) since such an obviousness rejection would be redundant with those stated further infra.

The prior art rejection under 102 based upon Krsmanovic et al, due to applicant's amendment of claim 1.

The prior art rejection under 102 of claim(s) based upon Marinkovich, due to applicant's amendment of claim 1.

The prior art rejection under 102 based upon Pouletty, due to applicant's amendment of claim 1.

The prior art rejection under 102 based upon Cowan, due to applicant's amendment of claim 1.

The prior art rejection under 103 based upon Marinkovich, Pouletty, or Cowan in view of Rhodes, due to applicant's amendment of claim 1.

The obviousness-type double patenting rejection of claim(s) 1-19 over the copending claims of US Application Ser. No. 10/696,770, since the copending claims have been amended such that the second binding site is a polypeptide.

Rejections of record that have been maintained are repeated as follows:

REJECTION(S) UNDER 35 USC 112, SECOND PARAGRAPH

Claims 16-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 16, lines 4 and 6, "the immune response component" lacks antecedent basis in claim 1. Since one does not know what the "immune response component" is, one also does not know what references to its "epitopes" at lines 4 and 6 means.

As previously noted, references to "different epitopes on the immune response component" and to "same epitopes on the immune response component" are unclear, because the "immune response components" would not be understood by one of skill as having any "epitopes". It is taken that "the immune response component" can be an antibody or a T/B cell receptor (see para. [0041] of applicant's disclosure in US 2004/0185054). It is well known in the art that these antibodies or T-cell receptors would recognize B or T epitopes on the antigenic components serving as "the first binding sites". The "epitopes" are thus on "the first binding sites", rather than on "the immune response component".

Applicant has not addressed this ground of rejection.

REJECTION(S) UNDER 35 USC 102/103

As stated in the action mailed on 9/8/06, for purposes of stating prior art rejections, the Office considers that the instant claims have benefit of the instant filing date of 1/9/04. Instant claim 1 recites specifics not disclosed in parent application 10/696,770. Instant claim 20 recites a newly disclosed concept of increasing a humoral immune response against a target that normally elicits a cellular immune response.

Applicant has not responded to this position of the Office. Instead applicant has urged that grandparent application 10/178,046 supports the instant claims. It is even more certain that grandparent application 10/178,046 fails to support the instant claims because it discloses far less that parent application 10/696,770. All of applicant's urgings, that point to parallel language in 10/178,046, are not convincing. While parallel or identical language might be found in various sections in the disclosure of 10/178,046,

this language does not, in fact, mean what it presently means. The instant teachings contemplate numerous embodiments that were not contemplated in grandparent application 10/178,046. For example, the term "immunity" presently encompasses "innate immunity" which was not contemplated in grandparent application 10/178,046. While such newly disclosed embodiments might have been obvious to one of skill, obviousness does not provide a proper basis for descriptive support under 35 USC 112. The description requirement is separate from the enablement requirement of 112, first para. (Vas Cath v. Mahurkar 19 USPQ2d 1111); and the description requirement cannot be satisfied by urging what might be obvious (Lockwood v. American Airlines 41 USPQ2d 1961).

Claims 1-2, 4, 13-15 and 21 are rejected under 35 U.S.C. 102(b) or (e) as being anticipated by Low et al (US 2001/0031252 or US 7,033,594).

Low et al teach therapeutic methods in which a "ligand- immunogen conjugate" is administered to a host. The ligand-immunogen conjugate corresponds to the instant "immunity Linker". The ligand component of this conjugate corresponds to the instant "second binding site". The ligand of Low et al serves to target the conjugate to pathogenic cells, such as cancer cells or foreign pathogen cells; Low et al teach that the ligand can be a "tumor-specific aptamer" (col. 8, line 8). The immunogen of Low et al corresponds to the instant "first binding site". See '594 at col. 1, lines 13-21; col. 2, line 37-col. 3, line 19; col. 3, lines 41-63; col. 6, lines 13-32, for example. From the above instant claim 1 is anticipated.

Regarding instant claim 2, note '594 at col. 10, lines 15-23 teaching immunization/vaccination to induce a pre-existing host immune response.
For instant claims 4 and 21, note '594 at col. 10, lines 23-26 teaching that the pre-existing host immune response may be an innate response against the alpha-gal group.

Regarding instant claim 13, note '594 at col. 1, Lines 25-44.

Regarding claims 14-15, note col. 9, lines 23-27 and col. 9, line 64-co1.10, line 2 teaching that the immunogen member of the conjugate may serve to redirect humoral or cellular immune responses in the host.

Applicant has urged that Low et al do not teach aptamers; however, as noted supra Low et al do teach aptamers as the ligand at col. 8, line 8. It was not necessary for the Office to have previously pointed out this teaching, since no claim has previously recited "aptamer".

Claims 1 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Low et al in view of Rhodes (4,940,670).

The primary reference has been cited supra against claim 1.
This shows treatment of cancer with a conjugate that corresponds to the instant "immunity linker" for the case in which the instant "second binding site" is an aptamer directed against cancer cells.

Rhodes teaches the therapeutic treatment of cancer patients with immunoconjugates that have a therapeutic agent (e.g. a radionuclide) conjugated to an antibody directed to an antigen on cancer cells. Rhodes teaches that, because tumor cells are heterogeneous in their expression of various individual tumor antigens, it is advantageous to use a cocktail of immunoconjugates; each of the immunoconjugates forming such a cocktail has an antibody specific for a different antigen known to be present in the cancer patient's tumor.

It would thus have been obvious to have used a cocktail (i.e. a "population") of "immunity linkers" taught by the primary reference, wherein the cocktail would contain various "immunity linkers" that differ from one another by virtue having different aptamers directed to different tumor cells that are present in a patient's tumor. By so doing one would have expected to be able to more effectively target tumors that have a heterogeneity in expression of tumor markers.

Furthermore, the Office finds motivation for use of such a cocktail, since Low et al teach (col. 9, lines 6-9) that one can use "combinations of ligand-immunogen conjugates to maximize targeting of the pathogenic cells for elimination". While Low et al give no further information about the composition of such combinations, it is considered that the teachings of Rhodes would have given one adequate direction in teaching one how to "maximize targeting of pathogenic cells" that are cancer/tumor

cells. It is further noted that, while Rhodes et al teach cocktails of different antibodies that are specific for different tumor antigens and the instant claims require a cocktail of immunity linkers that have different aptamers that are specific for different tumor cells, the functional equivalence of antibodies and aptamers as specific targeting ligands for tumor cells is implicit from the teachings of Low et al at col. 8, lines 5-12.

As in the case of the 102 rejection of record, Applicant has urged that Low et al do not teach aptamers; however, as noted supra Low et al do teach aptamers as the ligand at col. 8, line 8.

DOUBLE PATENTING

Claims 1-4, 7, 13 and 15-18 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8-13 of copending Application No. 11/606,564 (which is a CON of 10/178,046). Although the conflicting claims are not identical, they are not patentably distinct from each other because both the instant claims and the copending claims are drawn to "increasing an immune response" (i.e. "immunizing") an individual against a target by using a "immunity linker molecule". The instant claims are broad because, in the immunized individual, any of the innate, the cellular or the humoral immune response may be increased. The copending claims are narrow, because the immunized individual is required to have a "pre-existing antibody" (i.e. a pre-existing humoral immune response) against the first site of the linker; thus, in the immunized individual, the humoral response would be increased. The copending claims clearly encompass the use of an immunity linker which has an aptamer as the second binding site (e.g. claim 13). The instant broadly recited claims 1-4, 7, 13 and 15-18 encompass the more narrowly recited copending claims. Instant claim 15 and copending claim 8 are both drawn to a method of increasing a humoral response and thus encompass common subject matter. For these reasons a disclaimer is required.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The above is a restatement of the rejection in the action of 9/8/06, that provisionally rejected Claims 1-13 and 15-19 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 8 and 10-13 of copending Application No. 10/178,046. Though applicant has urged that application 10/178,046 has been abandoned, the rejection is maintained over the pending method claims of CON 11/606,564, in which claims 8 and 10 –13 have been amended by a preliminary amendment to be recited exactly as they were recited in parent 10/178,046, when the action of 9/8/06 for the instant application was mailed.

Applicant's arguments filed 3/8/07 have been fully considered but they are not persuasive for the above reasons.

Applicant's amendment has necessitated the following new ground(s) of rejection.

REJECTION(S) UNDER 35 USC 112, SECOND

Claims 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In each of claims 16 and 18, in the embodiment in which there is "one" immunity linker, it is unclear how "one" immunity linker could have "first binding sites that differ..." or second binding sites that differ...", respectively.

REJECTION(S) UNDER 35 USC 103

Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Low et al, in view of applicant's admitted state of the art (page 14, lines 10+).

Low et al have been cited supra as anticipating claim 1 for the embodiment in which the ligand-immunogen conjugate of Low et al, which corresponds to the instant "immunity linker", has a targeting ligand that can be a "tumor-specific aptamer" (col. 8, line 8).

Regarding instant claim 7, note '594 at col. 6, line 54-col. 7, line 37 and col. 8, Lines 27-37 teaching that the target cells may be various pathogens and teaching specific ligands for the pathogens. While Low et al do not specifically teach "aptamers" as a targeting ligand for microbial pathogens; it is taken that, from their teachings concerning the use of aptamers as a targeting ligand for tumor cells, one would have found it obvious to have used aptamers a targeting ligand for microbial pathogens. This is because the SELEX method of obtaining an aptamer that is specific for virtually any ligand was well known at the time of applicant's invention, and because such obtained aptamers were taught as being functionally equivalent to other art known receptors/ binders (e.g. antibodies, cell surface receptors, lectins) for binding to ligands. One thus would have found it obvious to have used aptamers to target microbial pathogens, in the same manner that Low et al taught the use of aptamers to target tumor cells.

At the time of second action, the examiner does not have the time to consider the prior art noted by applicant in detail. However, the examiner considers that any and all of the references cited by applicant at page 14, lines 15-19 and lines 30-32 are applicable as secondary references, without statement of a new ground of rejection, in the event that applicant should appeal these claims and argue further points concerning what the prior art of SELEX technology teaches.

Claims 1, 2, 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krsmanovic et al (5,378,815) in view of Low et al.

Krsmanovic et al teach a method of immunizing against target cancer cells. They use a "conjugate" which corresponds to the instant "immunity linker" The "targeting agent" component of this conjugate corresponds to the instant "second binding site". The "sensitizing agent" component of this conjugate corresponds to the instant "first binding site". See col. 2, lines 18-col. 3, line 30; col. 4, line 26- col. 5, line 14, for example. The "targeting agent"/"second binding site" of Krmanovic et al can be a "hormone such as insulin which binds specifically to receptors on the cell surface" (col. 6, lines 27-36). Krsmanovic et al do not teach a method in which the "targeting agent"/"second binding site" is an aptamer.

Low et al have been cited supra for showing immunization against cancer cells with the use of an Immunity linker" which has a "second binding site" which is an aptamer directed against cancer/tumor cells. Low et al also teach that the "second binding site" can be insulin and various other ligands of cell surface receptors on cancer/tumor cells (col. 8, lines 1-26). Since Low et al show the functional equivalence of an aptamer or insulin (and other ligands of cell surface receptors) as a "targeting agent"/ "second binding site", it would have been obvious to have used an aptamer as the "targeting agent"/ "second binding site" in the "conjugates"/"immunity linkers" of Krsmanovic et al. Instant claim 1 thus would have been obvious.

Regarding claim 2, note col. 4, lines 51-65.

Regarding claim 13, note col. 4, line 65-col. 5, line 5.

Regarding claim 15, the teaching that the "sensitizing" component (e.g. a toxoid antigen) of the "conjugate" binds to pre-existing antibodies thereto (e.g. see col. 4, lines 34-50) is consistent with the goal of increasing the patient's humoral immune response.

Claims 1-3 and 13-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marinkovich (US 2003/0108555) in view of Low et al.

Marinkovich teaches a method of immunizing/vaccinating against target cancer cells, so that cellular immunity against the cancer cells is enhanced. He uses a "conjugate" which corresponds to the instant "immunity linker". This conjugate can contain a monoclonal antibody that recognizes cancer cells; this antibody corresponds to the instant "second binding site". The antigen component of this conjugate corresponds to the instant "first binding site". See para. [0014]-[0018] and [0039]-[0053], for example. Marinkovich does not teach a method in which the "second binding site" is an aptamer.

Low et al have been cited supra for showing immunization against cancer cells with the use of an Immunity linker" which has a "second binding site" which is an aptamer directed against cancer/tumor cells. Low et al also teach that the "second binding sites" can be a "tumor-specific monoclonal or polyclonal antibodies" (col. 8, lines 1-10). Since Low et al show the functional equivalence of aptamers and antibodies, it

would have been obvious to have used an aptamer as the "second binding site" in the "conjugates"/"immunity linkers" of Marinkovich. Instant claims 1 and 14 thus would have been obvious.

Regarding claim 2, note para. [0016]. Regarding claim 3, note para. [0047] teaching that the Asp fl antigen can be either in purified form or recombinant form. Regarding claim 13, note para. [0001] teaching that cancer patients mount an ineffective immune response to cancers.

Claims 1-4, 13-18 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pouletty (WO 97/37690 or US 2006/0002891) in view of Low et al.

Pouletty teaches therapeutic methods that involve administering conjugates designated as "complexines" to a host. Such "complexines" correspond to the instant immunity linker. The complexines include a target binding moiety that corresponds to the instant "second binding site". The complexines also include a "selective member" that binds/interacts with a member of the immune system; this "selective member" corresponds to the instant "first binding site". The target binding moiety of Pouletty can be a ligand for a cell surface receptor, such as folate or various growth factors. The "selective member" of Pouletty can be an antigen to which to which the host has previously formed antibodies or T-cells. See, for example, para. [0018]-[0023]. Pouletty does not teach a method in which the "targeting agent"/"second binding site" is an aptamer.

Low et al have been cited supra for showing immunization against cancer cells with the use of an Immunity linker" which has a "second binding site" which is an aptamer directed against cancer/tumor cells. Low et al also teach that the "second binding site" can be folate or various other ligands of cell surface receptors on cancer/tumor cells (col. 8, lines 1-26). Since Low et al show the functional equivalence of aptamers and folate (and other ligands of cell surface receptors as a "targeting agent"/"second binding site", it would have been obvious to have used an aptamer as the "targeting agent"/"second binding site" in the "complexines"/"immunity linkers" of Pouletty. Instant claim 1 thus would have been obvious.

Regarding claim 2, note teachings of host immunity against the "selective member" by virtue of immunizations in para [0023].

Regarding claim 3, note para. [0023] teaching that the "selective member" of the conjugate may be an anti-idiotypic antibody. In such case the antigen that has been used to sensitize the host and the anti-idiotypic antibody constitute "immunological equivalents" in that both would bind to pre-existing antibodies formed in the host.

Regarding claims 4 and 21, note teachings of host immunity against blood group antigens in para. [0023] and against alpha-gal epitopes in para [0024] and [0026].

Concerning claim 13, note para. [0005]-[0006].

Regarding claims 14-15, note para. [0023] teaching that the selective member may bind to preexisting antibodies or to a T-cell. These selective members would thus serve, respectively, to enhance humoral or cellular immune responses in the host. Regarding claims 16 and 18, note para. [0027]-[0028].

Regarding further dependent claim 17, note that, when the A+B+vaccine Ag is used as the therapeutic agent, the host would have preformed, natural antibodies against the A and/or B antigen.

Also, regarding claim 18, note Pouletty at Example 4. Therein the "complexine" conjugate has its target binding moiety constituted by a polyclonal anti-thymocyte globulin preparation (para. [0050]). Any polyclonal antibody preparation is inherently heterogeneous in its specificity (i.e. many epitopes on the thymocyte cell surface will be bound) and in its binding avidity. Thus both conditions a) and b) of instant claim 18 are met.

Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pouletty (WO 97/37690 or US 2006/0002891) in view of Low et al and further in view of applicant's admitted state of the art (page 14, lines 10+).

Pouletty, as a primary reference, and Low et al, as a secondary reference have been cited supra as anticipating claim 1 for the embodiment in which the ligand-immunogen conjugate of Low et al, which corresponds to the instant "immunity linker", has a targeting ligand that can be a "tumor-specific aptamer" (col. 8, line 8).

Regarding instant claim 7, note Low et al ('594) at col. 6, line 54-col. 7, line 37 and col. 8, lines 27-37 teaching that the target cells may be various pathogens and teaching specific ligands for the pathogens. Note also, that Pouletty teaches immunization against microbial pathogens at para. [0030]. While Low et al do not specifically teach "aptamers" as a targeting ligand for microbial pathogens; it is taken that, from their teachings concerning the use of aptamers as a targeting ligand for tumor cells, one would have found it obvious to have used aptamers a targeting ligand for microbial pathogens. This is because the SELEX method of obtaining an aptamer that is specific for virtually any ligand was well known at the time of applicant's invention, and because such obtained aptamers were taught as being functionally equivalent to other art known receptors/ binders (e.g. antibodies, cell surface receptors, lectins) for binding to ligands. One thus would have found it obvious to have used aptamers to target microbial pathogens, in the same manner that Low et al taught the use of aptamers to target tumor cells, when using the "complexines" of Pouletty.

The Office considers that any and all of the references cited by applicant at page 14, lines 15-19 and lines 30-32 are applicable as secondary references, without statement of a new ground of rejection, in the event that applicant should appeal these claims and argue further points concerning what the prior art of SELEX technology teaches.

Claims 1-2 and 13-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cowan (WO 01/32207) in view of Low et al.

Cowan teaches therapeutic treatments involving the use of a hapten -ligand conjugate, which corresponds to the instant "immunity linker". The hapten portion of this conjugate corresponds to the instant "first binding site"; the individual being treated has been previously immunized against the hapten. The ligand portion of the conjugate corresponds to the instant "second binding site"; this can be an antibody or fragment thereof directed against a target antigen. See, for example, pages 6-7. This antibody can be used to target pathological cells, such as tumor/cancer cells (e.g. pages 7 and 8

and claims 6 and 9-10). Cowan does not teach a method in which one uses a targeting agent that is an aptamer.

Low et al have been cited supra for showing immunization against cancer cells with the use of an "immunity linker" which has a "second binding site" which is an aptamer directed against cancer/tumor cells. Low et al also teach that the "second binding sites" can be a "tumor-specific monoclonal or polyclonal antibodies" (col. 8, lines 1-10). Since Low et al show the functional equivalence of aptamers and antibodies, it would have been obvious to have used an aptamer as the "second binding site" in the "conjugates"/"immunity linkers" of Cowan. Instant claims 1, 2 and 18 thus would have been obvious.

Regarding claim 13, note page 4, para. (5).

Regarding claims 14-15, note Example 4 (pgs 11-12) teaching that one can administer a hapten-ligand conjugate which has the hapten DNP, which is recognized by antibodies of the humoral immune system of the individual/subject. Alternatively, one can administer a hapten-ligand conjugate which has the hapten ABA-Tyr, which is recognized by cellular immune system of the individual/subject. Thus a subject administered one of these conjugates achieves either humoral or cellular immunity, respectively, to the target antigen.

Regarding claim 16, note Example 4 (pgs 11-12) teaching that one can administer two hapten-ligand conjugates. One conjugate has the hapten DNP, which is recognized by antibodies of the humoral immune system of the individual/subject. The other conjugate has the hapten ABA-Tyr, which is recognized by cellular immune system of the individual/subject. Thus a subject administered both of these conjugates achieves both humoral and cellular immunity to the target antigen. Since the humoral and cellular immune systems involve different "immune response components" the limitations of claim 16 are met, to the extent that the examiner can understand claim 16 (see 112, second rejection supra).

Claims 1 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cowan (WO 01/32207) in view of Low et al and further in view of applicant's admitted state of the art (page 14, lines 10+).

Cowan, as a primary reference, and Low et al, as a secondary reference have been cited supra as anticipating claim 1 for the embodiment in which the ligand-immunogen conjugate of Low et al, which corresponds to the instant "immunity linker", has a targeting ligand that can be a "tumor-specific aptamer" (col. 8, line 8).

Regarding instant claim 7, note Low et al ('594) at col. 6, line 54-col. 7, line 37 and col. 8, lines 27-37 teaching that the target cells may be various pathogens and teaching specific ligands for the pathogens. Note also, that Cowan teaches immunization against microbial pathogens (e.g. pages 7 and 8 and claims 6 and 9-10). While Low et al do not specifically teach "aptamers" as a targeting ligand for microbial pathogens; it is taken that, from their teachings concerning the use of aptamers as a targeting ligand for tumor cells, one would have found it obvious to have used aptamers a targeting ligand for microbial pathogens. This is because the SELEX method of obtaining an aptamer that is specific for virtually any ligand was well known at the time of applicant's invention, and because such obtained aptamers were taught as being functionally equivalent to other art known receptors/ binders (e.g. antibodies, cell surface receptors, lectins) for binding to ligands. One thus would have found it obvious to have used aptamers to target microbial pathogens, in the same manner that Low et al taught the use of aptamers to target tumor cells, when using the conjugates of Cowan.

The Office considers that any and all of the references cited by applicant at page 14, lines 15-19 and lines 30-32 are applicable as secondary references, without statement of a new ground of rejection, in the event that applicant should appeal these claims and argue further points concerning what the prior art of SELEX technology teaches.

Claim 18 is rejected under 35 U.S.C. 103(a) as being unpatentable over any of Krsmanovic et al, Marinkovich et al, Pouletty or Cowan in view of Low et al as applied to claim 1 above, and further in view of Rhodes (4,940,670).

Each primary reference has been cited supra, in combination with Low et al, against claim 1. Each combination shows treatment of cancer with a conjugate that corresponds to the instant "immunity linker" for the case in which the instant "second binding site" is an aptamer directed against cancer cells.

Rhodes teaches the therapeutic treatment of cancer patients with immunoconjugates that have a therapeutic agent (e.g. a radionuclide) conjugated to an antibody directed to an antigen on cancer cells. Rhodes teaches that, because tumor cells are heterogeneous in their expression of various individual tumor antigens, it is advantageous to use a cocktail of immunoconjugates; each of the immunoconjugates forming such a cocktail has an antibody specific for a different antigen known to be present in the cancer patient's tumor.

It would thus have been obvious to have used a cocktail (i.e. a "population") of "immunity linkers" taught by the primary reference, wherein the cocktail would contain various "immunity linkers" that differ from one another by virtue having different aptamers directed to different tumor cells that are present in a patient's tumor. By so doing one would have expected to be able to more effectively target tumors that have a heterogeneity in expression of tumor markers.

Furthermore, the Office finds motivation for use of such a cocktail, since Low et al teach (col. 9, lines 6-9) that one can use "combinations of ligand-immunogen conjugates to maximize targeting of the pathogenic cells for elimination". While Low et al give no further information about the composition of such combinations, it is considered that the teachings of Rhodes would have given one adequate direction in teaching one how to "maximize targeting of pathogenic cells" that are cancer/tumor cells. It is further noted that, while Rhodes et al teach cocktails of different antibodies that are specific for different tumor antigens and the instant claims require a cocktail of immunity linkers that have different aptamers that are specific for different tumor cells, the functional equivalence of antibodies and aptamers as specific targeting ligands for tumor cells is implicit from the teachings of Low et al at col. 8, lines 5-12.

In summary, all of the above grounds of rejection over the prior art are based on the fact that Low et al have shown that aptamers were known targeting agents, that correspond to the instant "second binding site". Low et al have taught that aptamers were functionally equivalent to other known targeting agents, such as antibodies or ligands of cell surface receptors. While Low et al particularly taught aptamers as targeting agents for tumor cell surfaces, the use of aptamers as targeting agents for other kinds of pathological cells/agents, such as microbial pathogens, would have been fully obvious, since applicant has admitted (pg 14, lines 20-25) that SELEX technology can provide aptamers "that bind specifically with virtually any chemical compound." The mere fact that applicant has happened to name one type of "second binding site" that was known in the art, but that was only recited by one of the previously cited references, does not provide a basis for patentability. That the inventors who wrote other references might not have bothered to recite "aptamers" is not relevant, since a proper obviousness rejection assumes that applicant would have been aware of the full scope and contents of the prior art, including the prior at of Low et al.

Applicant's arguments filed 3/8/07 have been fully considered but they are not persuasive for the above reasons.

FINALITY

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONTACTS

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, whose telephone number is 571-272-0849. The examiner can normally be reached on Mon.-Thu. from 8:00 am to 5:30 pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Typed 5/29/07 DAS

David A Saunders

DAVID A. SAUNDERS
PRIMARY EXAMINER